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A Study of Physiological Mechanisms and Inter-Relations Between Systemic and Regional Blood Volume, Blood Flow and Electrolyte Balance

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(1) Regulation of Sodium Excretion

a) Effects of fasting and re-feeding

The effects of fasting and re-feeding with carbohydrate upon sodium excretion were investigated in young, healthy obese volunteers, who were hospitalized and maintained on a constant sodium, potassium and water intake. A water diuresis was induced during an equilibration period, again after 3 days of fasting and after 3 days of carbohydrate re-feeding. During starvation, insulin clearance, rate of sodium excretion, and osmolal clearance increased significantly, while the ratio of urinary volume to glomerular filtration rate was unaltered and the ratio of free water clearance to urinary volume decreased significantly. After 3 days of carbohydrate re-feeding, a water diuresis resulted in a significant fall in rate of sodium excretion, ratio of urinary volume to glomerular filtration rate, and osmolal clearance, whereas ratio of free water clearance to urinary volume increased significantly. When carbohydrate was fed at the peak of the water diuresis of starvation, the ratio of urinary volume to glomerular filtration rate decreased significantly within one hour.

These studies suggest that the natriuresis of starvation may be attributed to a decrease in distal tubular reabsorption and that the re-feeding of carbohydrate induces antinatriuresis by enhancing proximal tubular reabsorption. The sodium retention observed after several days of carbohydrate re-feeding may be attributed to increased proximal and distal tubular reabsorption.

b) Relationship of valvular disease to sodium excretion

Previous studies under this grant indicated that an early manifestation of mitral valvular disease may be an abnormally increased retention of a sodium load. This contrasts sharply with patients with systemic hypertension, which long have been known to manifest an increased excretion of a sodium load. Toor and associates, some time ago, postulated that increased intraventricular pressure might be responsible for the latter phenomenon and reported some observations in confirmation of this hypothesis.

Recently, we had the opportunity to study two patients with aortic stenosis and increased intraventricular pressure. Excretion of a sodium load was indeed normal to increased, notwithstanding evidence of heart failure. Further studies of this phenomenon are being planned.

c) Effects of atrial tachycardia and atrial fibrillation

Previous studies of the effect of atrial tachycardia and atrial fibrillation upon renal hemodynamics and sodium excretion have been extended, using the previously described experimental protocol in dogs. Measurements were made in 11 dogs during normal sinus rhythm and, at comparable rates, with atrial pacing and atrial fibrillation. Changes from normal sinus rhythm to atrial pacing resulted in significant decreases in sodium excretion (20% from 464 μEq/min), in renal blood flow (11% from 282 ml/min) and in blood pressure (10% from 127 mm Hg). Cardiac output and glomerular filtration rate did not show any consistent changes. In responses to changing from atrial pacing to atrial fibrillation, there were further significant decreases in urinary sodium excretion (13%), renal blood flow (9%), and blood pressure (7%), as well as a significant fall in cardiac output (21% - 1.8 L/min). Glomerular filtration rate continued stable. Changes in urinary sodium excretion correlated significantly with changes in blood pressure ($r = + 0.84$) throughout all conditions. In contrast, changes in cardiac output and renal blood flow correlated poorly with changes in urinary sodium excretion.

It has thus been established that both atrial tachycardia and atrial fibrillation may be accompanied by significant reductions in urinary sodium excretion. The data suggest that mean arterial pressure is a major factor in the changes in tubular reabsorption of sodium associated with altered atrial rhythm.

(2) The Circulatory Response to Orthostatic Stress in Man

a) The role of circulatory congestion

The role of circulatory congestion in the increased tolerance of orthostatic stress, previously observed in patients with heart failure, was evaluated. Five patients with heart failure were studied hemodynamically in the supine and upright positions. These patients were able to maintain cardiac index and stroke volume with only an insignificant increase in heart rate (6%). Peripheral vascular resistance and arteriovenous oxygen difference did not change significantly.

These results contrasted with 6 normal subjects who underwent orthostatic stress before and after volume expansion, with 10% low molecular weight dextran or normal saline. Before infusion, the classical normal response to orthostatic stress was seen: cardiac index decreased by 22%, stroke volume decreased by 35% and heart rate increased by 29%. Arterial pressure was maintained by an increase of 43% in peripheral vascular resistance, and the arteriovenous oxygen difference widened by 52%. After infusion, the response to orthostatic stress fell between that of the pre-infusion and the heart failure patients. Cardiac index did not change significantly, whereas heart rate increased by only 7% and arteriovenous oxygen difference widened by only 26%, both significantly less than before infusion.

Orthostatic tolerance in normal subjects was thus improved by expansion of plasma volume. It may be concluded that circulatory congestion plays a major role in the increased tolerance of orthostatic stress shown by patients with heart failure.

b) <u>Resistance to bed rest deconditioning in patient with heart failure</u>

The previously described increased tolerance of orthostatic stress observed in patients with heart disease, and especially with heart failure, led to the hypothesis that such patients might be resistant to deconditioning by bed rest. Accordingly, the responses of heart rate, systolic and diastolic blood pressure to a 70° passive upright tilt were studied in 8 patients with congestive heart failure after four to 21 days of strict bed rest. Orthostatic stress was well tolerated. There was no significant change in heart rate (+8.3 beats/min) or systolic blood pressure (-0.9 mm Hg). The diastolic blood pressure increased by 6.7 mm Hg, narrowing the pulse pressure slightly. In 6 patients restudied after ambulation there was no significant difference between bed rest and ambulatory responses. Thus, in contrast to patients treated with bed rest for acute myocardial infarction, who in a previously described study showed a significant incidence of vasodepressor reactions to orthostatic stress, cardiovascular deconditioning was not observed in patients with congestive heart failure treated with strict bed rest.

(3) Development of a Miniature Pressure Transducer

Two pilot experiments have been carried out in collaboration with W. Rindner, A. Garfein, and A. Iannini of the NASA Electronics Research Center of Cambridge, Massachusetts to evaluate a miniature piezo - junction pressure transducer (tunnel diode). This device may provide a method for long term monitoring of blood pressure in patients, subjects, or experimental animals using indwelling intravascular or implantable transducers. The potential for miniaturization is great, since the pressure pickups may be as small as 1 mm diameter, and this may in turn allow chronic instrumentation with minimal trauma.

Current efforts have been directed toward testing the first two models of the device, to achieve the goals of baseline stability, temperature insensitivity, accurate DC level pressure recording, and durability and ruggedness. The two pilot studies, carried out in anesthetized dogs with the device mounted at the end of a conventional cardiac catheter, show that high fidelity intravascular pressure tracings may be obtained from various sites including the aorta and left ventricle. Further details are planned in acute and chronic animal experiments.

Publications

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